REMARKS/ARGUMENTS

Claims 1-11 and 13-16 are active in this application.

Claim 1 is amended to incorporate the definitions from Claim 12 and as a result Claim 12 is cancelled.

No new matter is added.

The pending claims in this application are directed to a multilayer dosage form of a pharmaceutical which includes a neutral core, an inner layer composed of a methacrylate polymer which itself is composed of particular (meth)acrylate monomers having particular properties, a specified outer core, and an active bound to the polymer of the inner core. As discussed in the application in the paragraph bridging pages 5-6, this formulation provided initial slow release (due to the outer layer) followed by a similar slow release of the active that was not affected by the ionic strength of the dissolution medium.

In the Office Action, the Examiner has maintained the rejections in view of Ulmius (US 5,643,602) with or without Beckert et al (WO 01/68058). The reasons the rejection has maintained the rejection are provided primarily on pages 3-4 of the Action. Briefly, the Examiner has not found Applicants prior arguments persuasive because (A) plasticizers and release agents are optional in Ulmius; (B) the NE polymers are suggested in Ulmius thereby making it obvious to use those polymers in the inner layer; and (C) the lack of effect in the different ionic strengths of the dissolution medium is alleged to be inherent in the formulation that results from the obvious combination in Ulmius.

Under U.S. law something that is alleged to be inherent must necessarily be so and the evidence provided in the specification shows that compositions also within the scope of Ulmius (following the Examiner's rationale) do not exhibit that ionic strength stability. The Examples provided in the specification, particularly Examples 5 and 6, demonstrate that inner

layers of particular types of polymer (Eudragit® RL 30D-having less than 90% by weight (meth)acrylate monomers) exhibit significantly different release rates under different ionic strengths unlike Eudragit® NE30 D-both of which are described in the Ulmius patent cited in the rejections.

Even in view of WO 01/68767 (see pages 4-5 of the specification) that the claimed formulation provided these advantages was not predictable.

Further, as also discussed in the specification on page 5, the inventors discovered that when inner methacrylate copolymer coating comprises at least 90% by weight of (meth)acrylate monomers having neutral radicals, wherein the methacrylate copolymer has a minimum film-forming temperature as specified in DIN 53 787 not exceeding 30°C, it is possible the active can be provided in the inner coating without the aid of excipients such as plasticizers or release agents as is typically the case in such formulations (see again WO 01/68767 and also the cited Ulmius patent; and new Claims 13-16).

Ulmius describes a multilayer drug delivery unit (see col. 5, lines 3-26) including any number of polymers, including Eudragit®-type polymers (see also the Examples). Col. 5 of Ulmius describes a first layer including many different types of polymers, including Eudragit® type polymers but none of the Examples in Ulmius describe polymers in the inner coat (or layer) that includes a polymer like that which is claimed). While the Examples use some of those Eudragit® polymers as the outer layer, the Examiner has determined that it would have been obvious to use any one of the Eudragit® polymers as an inner (or first) layer replacing the ethylcellulose (Aquacoat ECD30 is an aqueous dispersion of ethylcellulose[1]) as actually used by Ulmius.

Applicants disagree.

[1] See, e.g., www.fmcbiopolymer.com/pharmaceutical/Products/Aquacoat.

First, there is nothing in Ulmius which provides the necessary direction to specifically select the type of metacrylate polymer defined in the claims from amongst all the possible polymers that are described by Ulmius (see listing in col. 5, for example). Second, that the selection of the specific methacrylate polymer permitted slow release of the active that was not affected by the ionic strength of the dissolution medium (see Examples in the application) could not have been predicted based on what Ulmius described (see page 5, last ¶ of the present application).

As explained in MPEP 2145: "An "obvious to try" rationale may support a conclusion that a claim would have been obvious where one skilled in the art is choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success. " [A] person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1397 (2007).

However, as the evidence of record (in the specification) shows, reasonable prediction of success from the teachings of cited art are not present for the percentage release of active substance as defined in Claim 1 because the evidence shows that combinations within the teachings of Ulmius lead to compositions not meeting that definition. See also, *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd,* 533 F.3d 1353, 87 U.S.P.Q.2D 1452 (Fed. Cir. 2008): "To the extent an art is unpredictable, as the chemical arts often are, KSR's focus on these "identified, predictable solutions" may present a difficult hurdle because potential solutions are less likely to be genuinely predictable."

To reiterate, Examples 5 and 6 in the present application illustrate the point made above. That is Example 5 employs Eudragit® NE 30 D as inner coat (that is meeting the

definition provided in the claims) with an outer gastroresistant coating (Eudragit® L 30 D) whereas Example 6 uses an inner coat polymer Eudragit RL 30D, that is also described in Ulmius as a preferred polymer, see col. 5 and which does not meet the definition in the claims and having the same outer, gastroresistant coating (see page 33 of the specification). The release profiles of these two Examples are shown in FIGS 5 and 6 (reproduced below) with FIG 5 showing the release profile of Example 5 in different ionic medium, isotonic or hypotonic and FIG 6 showing the same analysis for the material in Example 6.

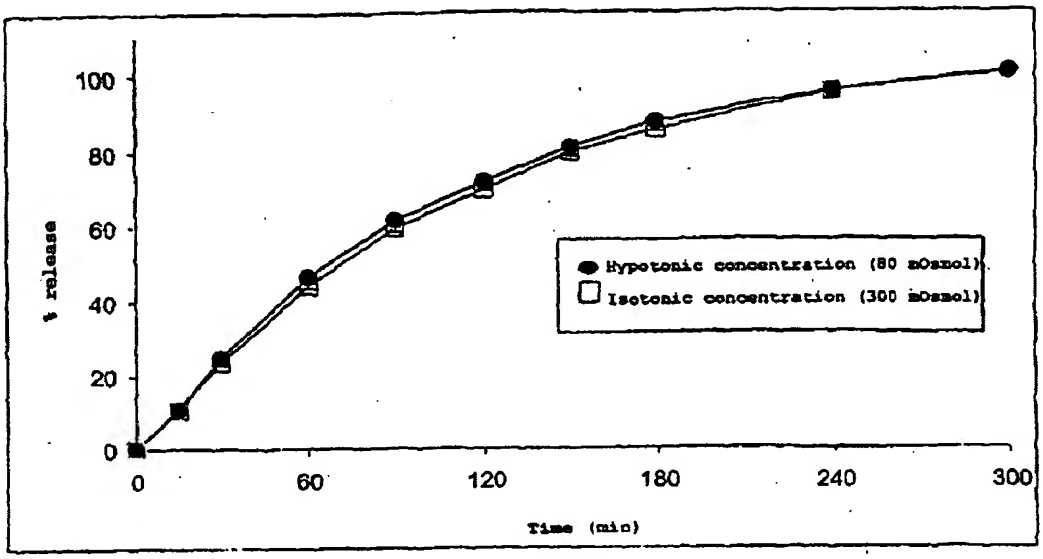


Fig. 5

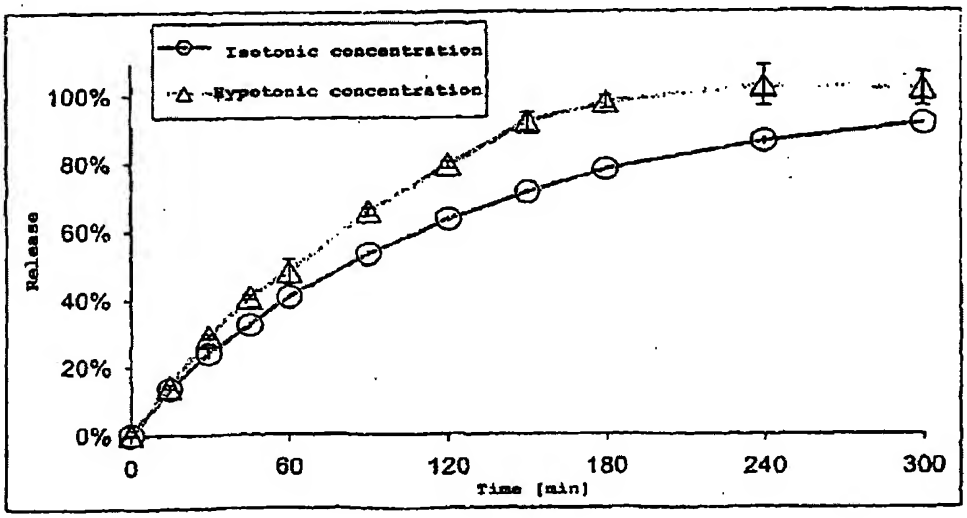


Fig. 6

As is clear from the figures, when the composition as defined in the claims was tested, the release profile remained relatively unchanged in the different ionic conditions, which was not the case for the composition in Example 6. Such an effect could not have been predicted based on what Ulmius described (see page 5, last ¶ of the present application).

Still further, with respect to claims 13-16, the selection of the specific methacrylate polymer enabled the active to be provided in the inner coating without the aid of excipients such as plasticizers or release agents as is typically the case in such formulations (see pages 4-5 in the specification citing to WO 01/68767, also the cited Ulmius patent. This is not at all suggested by Ulmius.

As the basis of the rejection is *prima facie* reasonable predictability and the evidence shows that this is not the case, it has not been established that the claims are obvious in view of the cited reference.

Further, the evidence rebuts any alleged *prima facie* case of obviousness, showing the improved results that the specification states would not have been reasonably predictable based on what is described in Ulmius.

Withdrawal of the rejection based on Ulmius is requested.

The Examiner has also rejected Claims 1-9 and 12 as being obvious in view of Ulmius combined with Beckert et al (WO 01/68058). Briefly, this rejection was raised primarily because Ulmius only describes glucocorticosteroids as the active and it for this that Beckert et al is cited. While Beckert does describe polymer coatings, e.g., methacrylate type polymers for the outer coating, Beckert does not alter the fact that what is described in Ulmius does not render the claims obvious and as a result the combination of the cited publications does not as well.

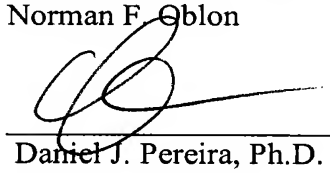
In addition, as discussed above, the percentage release of active substance as defined in Claim 1 is neither inherent in the compositions of the cited references (because under U.S. law, inherency requires necessity, something that the evidence clearly shows is not the case) nor reasonably predictable because the evidence shows that this is the case.

Withdrawal of the rejection is requested.

A Notice of Allowance is also requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Daniel J. Pereira, Ph.D.
Attorney of Record
Registration No. 45,518

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)